PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61M 15/00	A1	(11) International Publicati n Number: WO 97/04827
		(43) International Publicati n Date: 13 February 1997 (13.02.97)

(21) International Application Number: PCT/US96/12222

(22) International Filing Date: 25 July 1996 (25.07.96)

(30) Priority Data:
08/506,703 25 July 1995 (25.07.95) US

(71) Applicant: DAVID SARNOFF RESEARCH CENTER, INC. [US/US]; 201 Washington Road, CN 5300, Princeton, NJ 08543-5300 (US).

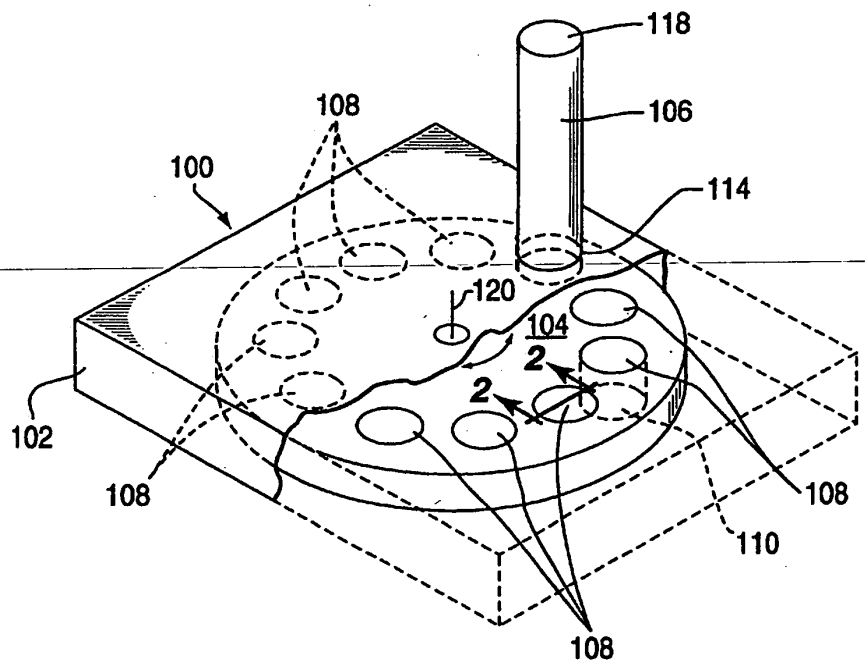
(72) Inventors: DATTA, Pabitra; 9 Yeger Road, Cranbury, NJ 08512 (US). DESAI, Nitin, V.; 7 Amherst Way, Princeton Junction, NJ 08550 (US).

(74) Agents: BURKE, William, J.; David Sarnoff Research Center, Inc., 201 Washington Road, CN 5300, Princeton, NJ 08543-5300 (US) et al.

(81) Designated States: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: INHALER APPARATUS USING A TRIBO-ELECTRIC CHARGING TECHNIQUE



(57) Abstract

A tribo-inhaler (100) having a container portion (104) for electrostatically retaining a predefined dose of medicament powder and extracting the medicament powder by inhaling air through the container portion.

INHALER APPARATUS USING A TRIBO-ELECTRIC CHARGING TECHNIQUE

The invention relates to medication inhalers and, more particularly, to apparatus for electrostatically retaining a medicament powder within an inhaler using a tribo-electric charging technique.

Inhalers are used to administer pre-determined quantities (doses) of inhalable dry powder medicament to the lungs of a patient. Generally, inhalers are mechanical systems that generate a metered cloud of medicament that is inhaled by a patient. Many of these prior art inhaler devices use chloroflourocarbon (CFC) gas to facilitate generation of the metered cloud of medicament. However, since CFCs are no longer used in consumer products, other techniques for generating the medicament cloud have been explored.

In U.S. patent 4,811,731, a non-CFC, prior art inhaler is disclosed which contains a plurality of measured doses of medicament stored in a blisterpack. Upon use, one of the blisters in the blisterpack is punctured and a patient inhales the medicament from the punctured blister via a mouthpiece of the inhaler. The medicament dosage varies with the amount of force with which the patient inhales. Since inhalation of a powder from a blisterpack is rather difficult and a patient does not repeatedly inhale with the same force each time the medication is taken, the medicament dosage that is actually consumed can vary greatly from dose to dose.

Thus, a need exists in the art for an inhaler that, over a wide range of inspirable flow rates, maximizes drug propagation to the lungs and provides, with each use of the inhaler, substantially identical doses of medicament to the lungs.

The invention overcomes the disadvantages associated with prior art inhalers by using a tribo-electric charging technique to retain a medicament powder within an inhaler apparatus. This unique inhaler apparatus has been dubbed a tribo-inhaler. The tribo-inhaler comprises a container portion within which is electrostatically retained a predefined dose of medicament powder, where the powder is tribo-electrically charged, and a mouthpiece or inhalation tube, attached to the container portion, for extracting the medicament powder from the container portion.

The teachings of the invention can be readily understood by considering the following detailed description in conjunction with the accompanying drawings, in which:

FIG. 1 depicts partial section, perspective view of a first embodiment of the tribo-inhaler;

FIG. 2 depicts cross-sectional view of a cavity within tribo-inhaler of FIG. 1;

FIG. 3 depicts a cross-sectional view of a tribo-electric charging apparatus for coating polymeric beads with powdered medicament; and

FIG. 4 depicts a exploded view of a second embodiment of the tribo-inhaler; and

FIG. 5 depicts a cross-sectional view of the second embodiment of the tribo-inhaler taken along line 5-5 of FIG. 4.

To facilitate understanding, identical reference numerals have been used, where possible, to designate identical elements that are common to the figures.

The invention is an inhaler apparatus containing one or more predefined doses of medicament powder. The invention retains each dose within a container portion by an electrostatic charge generated using a tribo-electric charging technique.

Specifically, FIG. 1 depicts a partial sectional view of a first embodiment of the tribo-inhaler 100. The tribo-inhaler 100 contains a housing 102 having a container portion 104 for retaining a medicament powder, and a flexible inhalation tube 106, attached to the housing, for extracting the medicament from the container portion. The container portion defines at least one cavity 108. Each cavity is an aperture 110 that passes through the container portion. The illustrative container portion 110 contains a plurality of cylindrical apertures that are evenly distributed in a circular pattern near the circumferential edge of the container portion. Medicament powder 112 is electrostatically retained within each cavity. The container portion 104 is moveable relative to the housing, e.g., in response to user manipulation, the container portion rotates about a central axis 120 thereof (indicated by arrow 116). More specifically, the container portion 104 is disk-shaped and is rotatable within the housing such that any one of the cavities can be positioned proximate one end (an inlet end 114) of the inhalation tube. The inhalation tube 106 has its inner surface coated with a material, such as Teflon, that reduces adhesion of the medicament to the tube as the medicament passes through the tube. Additionally, the inhalation tube 106 is generally flexible such that it easily folds along the top of the housing. As such, the inhaler easily fits within a shirt pocket or purse.

In use, a patient inhales through the outlet end 118 of the inhalation tube 106 to withdraw medicament from a selected cavity. To inhale subsequent doses, the container portion is rotated to position a different, unused cavity proximate the inlet end of the tube. Alternatively, a metered

quantity and flow rate of compressed air could be applied to the cavity to transport the medicament to the patient's lungs.

More specifically, FIG. 2 depicts a cross-sectional view of a single cavity 108 of the tribo-inhaler 100 taken along line 2-2 of FIG. 1. The cavity is essentially a cylindrical aperture 110 through the container portion 104. The first and second ends 200 and 202 of the aperture are respectively enclosed by a first and second screen 204 and 206. Each screen is approximately 200 mesh. Alternatively, the screens could be perforated solid layers of plastic or metal having openings with diameters of approximately 5 to 10 micrometers (μm).

The cavity contains at least one, and more typically, a plurality of beads 208. The surface of each bead is coated with a powder 112. The powder adheres to the bead surface by electrostatic attraction generated by a tribo-electric charging technique. The process and apparatus used to tribo-electrically charge the beads and powder is discussed below with respect to FIG. 3.

The container portion is fabricated by forming, typically by drilling, evenly spaced apertures in a disk-shaped substrate. Typically, the substrate is manufactured of plastic. Alternatively, the container portion is manufactured of injection molded plastic and the cavities are formed by the mold. Screen 206 (lower screen) is affixed to the surface of the container portion to close second aperture end 202. A select number of medicament coated beads are placed into the cavity, then the first screen 204 (upper screen) is affixed to the container portion surface to close first aperture end 200. The screens are typically affixed by an adhesive such as epoxy.

When a cavity is positioned proximate the inlet end of the inhalation tube and air is inhaled therethrough, air passes through the second screen, the cavity, and the first screen. As the air passes through the cavity, the beads are carried upwards until they impact the first screen. Since the beads impact the screen with substantial force, the medicament coating is dislodged from the surface of the beads. The dislodged medicament enters the inlet end of the inhalation tube as a cloud of medication and the tube carries the medicament to the patient that had inhaled on the outlet end of the inhalation tube. In this manner, a metered dose of medication is delivered to the patient's lungs.

FIG. 3 depicts apparatus for tribo-electrically charging a medicament powder 112 so that the powder adheres to a plurality of beads 208. Specifically, the apparatus contains an enclosed bead container 300 having a lid 302, a plurality of beads 208, and a medicament powder 112. The beads

and powder are mixed by shaking the container for one to ten minutes. During this period, the powder becomes tribo-electrically charged and the powder 112 electrostatically adheres to the beads 208.

More specifically, the beads have a diameter of between 50 and 200 μm and may be fabricated of one of the following materials Teflon, polyvinylidene fluoride, polypropylene, dyed polypropylene, flouro-treated glass, glass, amino-treated glass, polystyrene, titanium dioxide-filled polyethylene and the like. In use, the medicament and beads are added to the container 300, the lid of the container is closed and the beads and medicament mixture is shaken for one to ten minutes. During the shaking process, a charge accumulates on the particles of the powder. Once charged, the medicament particles uniformly coat the surface of each bead.

The amount and polarity of the charge on the medicament particles depends upon the fabrication material of the beads. By measuring the charge-to-mass ratio of the powder using a faraday cage, the inventors have found that by selecting a particular bead material the charge characteristics are controllable. For example, charging a mometasone furoate (MF) powder in a glass container using four beads having 100 μm diameters at 70 degrees Fahrenheit and 45% relative humidity, resulted in the charge-to-mass ratios for various bead materials shown in TABLE 1.

Bead Material	Charge Polarity	Ratio (ΔC/gm)
Teflon	positive	35
Polyvinylidene fluoride	positive	30
Polypropylene	positive	6.5
Dyed polypropylene	positive	10
Flouro-treated glass	positive	17.8
Glass	negative	6.5
Amino-treated glass	negative	39.8
Polystyrene	negative	42.7
Titanium dioxide-filled polyethylene	negative	7.7

TABLE 1 Charge-to-mass ratios for various bead materials

By appropriate selection of the bead material, the charge-to-mass ratio can be varied from 6.5 to 43 mC/gm and the charge is either positive or negative. When retaining a medicament, a low microgram quantity of medicament (e.g., 2-10 mg) requires a relatively high charge-to-mass ratio and a high microgram quantity of medicament (e.g., 20-40 mg) requires a relatively low charge-to-mass ratio. Thus, flexible charging characteristics are useful in facilitating retention of a wide range of medicament dosages.

Once the beads are coated with medicament, the coated beads are placed into a cavity of the container portion. A specific dose of medicament is defined by selecting a particular number of coated beads for placement in the cavity. When the medicament is dislodged and inhaled, a metered dose of medication is inhaled by the patient.

FIG. 4 depicts an exploded, perspective view of a second embodiment of the inventive tribo-inhaler 400. FIG. 5 is a cross-sectional view of the inhaler 400 taken along line 5-5 of FIG. 4. To best understand this embodiment of the invention, the reader should consult both FIGS. 4 and 5 while reading the following disclosure.

The inhaler 400 is an assembly having three main components; namely, a cover portion 402, a medicament container portion 404, and a outer housing 406. Each of the components is typically fabricated of injection molded plastic. The cover portion contains, affixed centrally to its top surface, a knob 414 and, affixed centrally to its bottom surface, a shaft 416. The shaft extends through a central bore 418 of the container portion 404 and is press fit therein. Additionally, the shaft rotatably extends through a central bore 420 in the outer housing 406. An end cap 422 is affixed, by gluing, welding, and the like, to the end of the shaft 416 such that the shaft can not be removed from the bore 420 but freely rotates therein. The cover portion and container portion rotate with respect to the outer housing about a central, longitudinal axis 436 of the shaft.

The medicament container 404 is substantially cylindrical and contains one or more cavities 408. Each cavity is substantially triangular in plan form having three walls and a bottom, where the top of the cavity is open to allow for the tribo-electrically charged beads (not shown) carrying the tribo-electrically charged medicament to be placed in the cavity. The bottom of the cavity contains an air inlet hole 424 that is covered with a mesh screen 426 having a mesh size that permits air to pass into the cavity but retains the beads within the cavity 408 (e.g., a mesh size of approximately 200 mesh). An outer circumferential wall 410 that forms one wall of each cavity defines a medicament extraction hole 412 into each cavity. These holes are covered by a mesh screen 428 located inside each cavity. Mesh screen 428 has a mesh size that retains the beads in the cavity, but permits the medicament to be extracted from the cavity (e.g., a mesh size of approximately 200 mesh).

The shaft 416 is press fit into bore 418 such that when knob 414 is rotated, the medicament container portion 404 rotates with respect to the outer housing 406. The outer circumferential edge of the cover portion

interfits a lip 438 located on the upper edge of the wall 410. The interfit of the cover portion and the container portion seals each cavity such that air may only ingress and egress the cavity through the screens. To facilitate a sufficient seal, an adhesive may be applied about the lip to affix the edge of the cover portion to the lip.

The outer housing contains a cylindrical outer wall 430 supported by a bottom portion 432. The bottom portion defines an air intake hole 434 that is positioned at a radial distance from the longitudinal axis 436 of the shaft that is equivalent to the radial distance of the air inlet hole 424 from the longitudinal axis of the shaft. As such, the air intake hole 434 can be aligned with a selected air inlet hole 424 by rotating the knob 414.

Additionally, the outer housing 406 contains an inhalation tube in the form of a mouthpiece 438 that extends from the outer wall 430. The mouthpiece bore has an inlet end 448 and an outlet end 446. The mouthpiece contains a bore 440 that extends longitudinally through the mouthpiece and through the wall 430. The mouthpiece bore 440 is aligned with the medicament extraction hole 412 located in the container portion 404. As such, by manipulating the knob, a particular cavity can be rotated into alignment with the mouthpiece. Alignment being defined as a cavity position that aligns the air inlet hole 434 with an air intake hole 424 and aligns a medicament extraction hole 412 with the mouthpiece bore 440. Once alignment has been attained for a selected cavity, a user (patient) inhales on the mouthpiece, drawing air through the air inlet and air intake holes and through the cavity. As the air passes through the cavity, the beads are moved toward extraction hole 412 and impact the screen 428. The impact dislodges the medicament from the beads, where the medicament is carried by the air flow through the mouthpiece bore and into the user's lungs. To facilitate alignment and use of particular cavities, the cover portion is typically labeled with cavity numbers (not shown) and each cavity has an associated alignment mark 442. To achieve alignment, a selected cavity's alignment mark 442 is aligned with a reference mark 444 on the mouthpiece or some other indicia of alignment. Alternatively, alignment can be achieved using a mechanical lock mechanism that engages a detent when alignment with a particular cavity is achieved.

Although various embodiments which incorporate the teachings of the invention have been shown and described in detail herein, those skilled in the art can readily devise many other varied embodiments that still incorporate these teachings.

What is claimed is:

1. An inhaler apparatus comprising:

a container portion for electrostatically retaining a predefined dose of medicament powder, where said medicament is tribo-electrically charged; and

an extracting means, attached to said container portion, for extracting said medicament powder from said container portion.

2. The apparatus of claim 1 wherein said container portion defines a cavity, said cavity contains at least one bead having, deposited upon a surface of the bead, a coating of said medicament powder, where said powder electrostatically adheres to said surface; a first screen and a second screen for enclosing at least one bead in said cavity and allowing gas to pass through said cavity.

3. The apparatus of claim 2 wherein said extracting means further comprises an inlet end and an outlet end, where said inlet end is positioned proximate said first screen and, inhaling through said extracting means, said medicament is dislodged from said bead and propagates from said inlet end to said outlet end.

4. The apparatus of claim 3 wherein said container portion defines a plurality of cavities.

5. The apparatus of claim 4 further comprising an housing for supporting said container portion and said extracting means, where said container portion is moveable relative to said housing and said extraction means to position any one of the plurality of cavities proximate said inlet end of said extraction means.

6. The apparatus of claim 5 wherein said container portion is rotatable relative to said housing and said extraction means.

7. Inhaler apparatus comprising:

a container portion defining a cavity;

said cavity containing at least one bead having, deposited upon a surface of the bead, a coating of medicament powder, where said powder electrostatically adheres to said surface;

a first screen and a second screen for enclosing at least one bead in said cavity and allowing a gas to pass through the cavity; and

extracting means for extracting said medicament powder from said cavity having an inlet end and an outlet end, where said inlet end is positioned proximate said first screen and, inhaling through said extracting means, said medicament powder is dislodged from said bead and propagates from said inlet end to said outlet end.

8. The apparatus of claim 7 wherein said container portion defines a plurality of cavities.

9. The apparatus of claim 8 further comprising a housing for supporting said container portion and said extracting means, where said container portion is moveable relative to said housing and said extracting means to position any one of the plurality of cavities proximate said inlet end of said extracting means.

10. The apparatus of claim 9 wherein said container portion is rotatable relative to said housing and said extracting means.

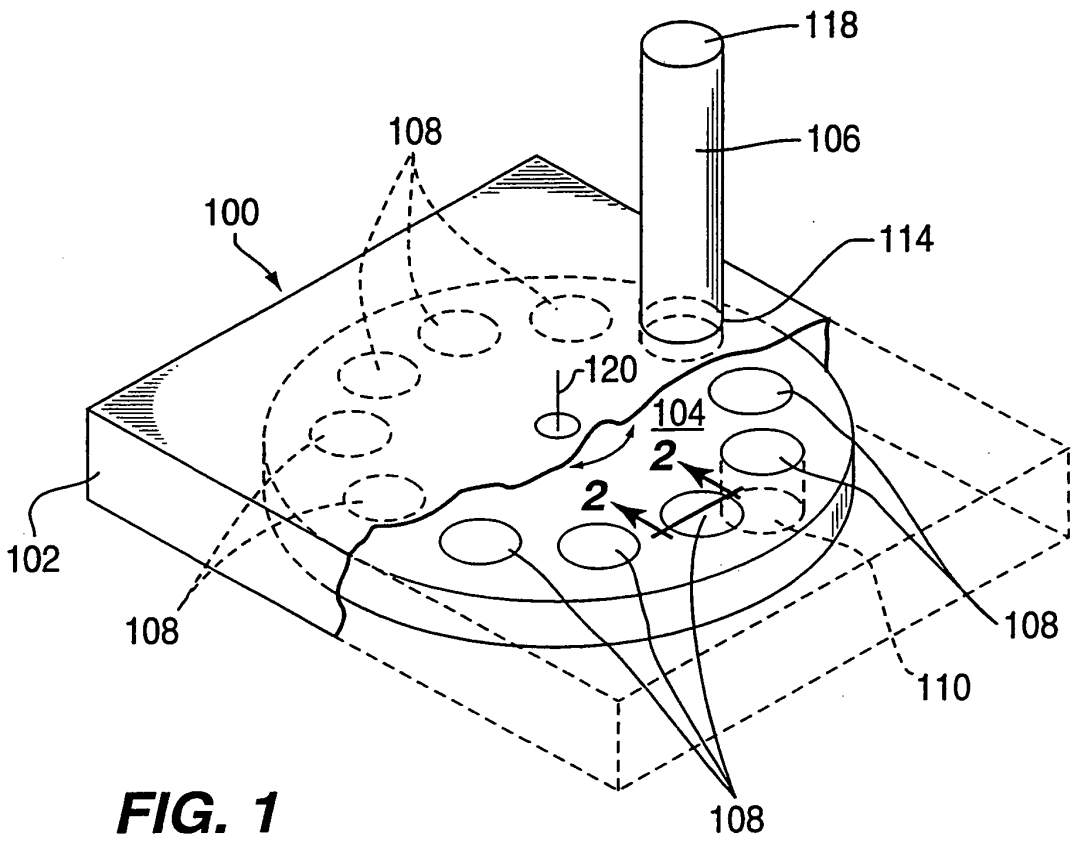

118
106
108
100
114
120
104
2
2
102
108
108
110
108

FIG. 1

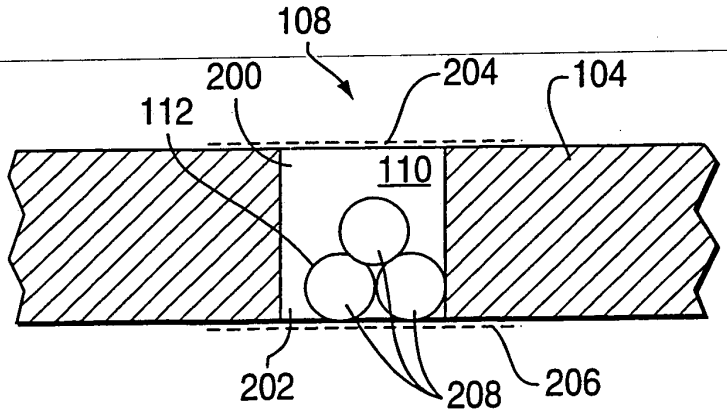

108
200
204
104
112
110
202
208
206

FIG. 2

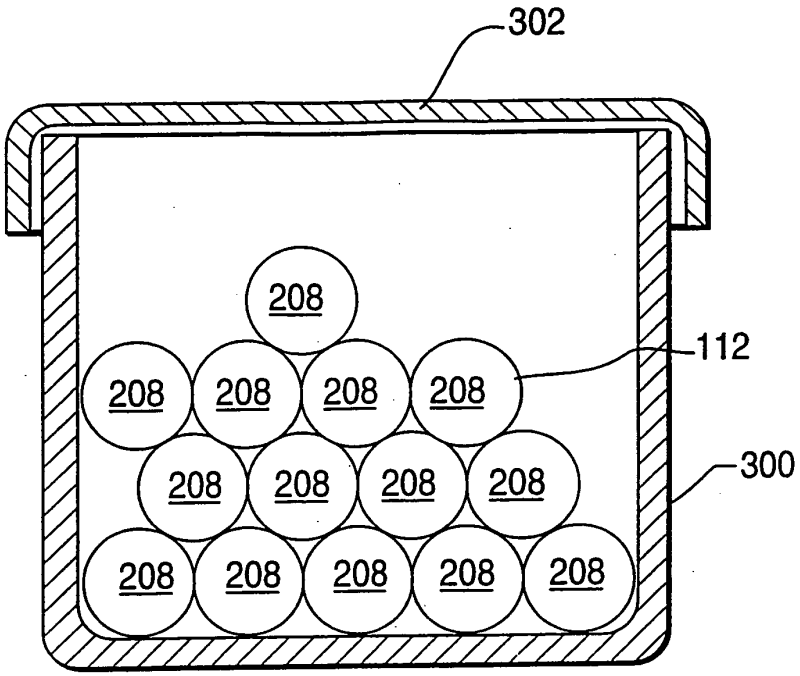

302
208
208
208
208
208
112
208
208
208
208
300
208
208
208
208
208

FIG. 3

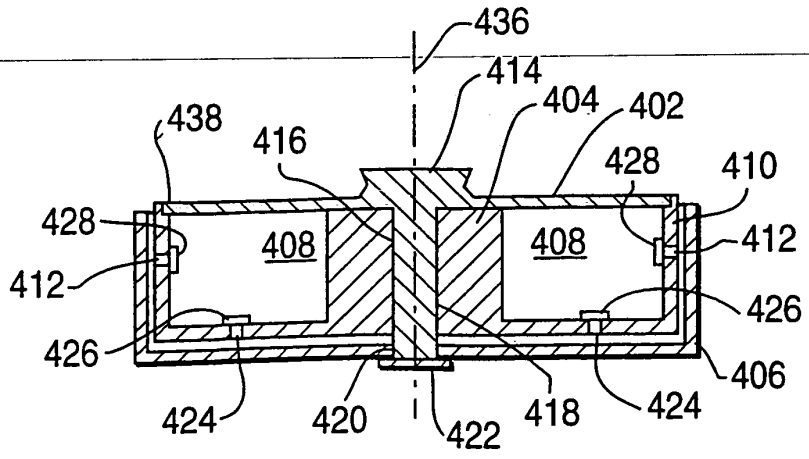

436
414
404
402
438
416
428
410
428
408
408
412
412
426
426
406
424
420
422
418
424

FIG. 5

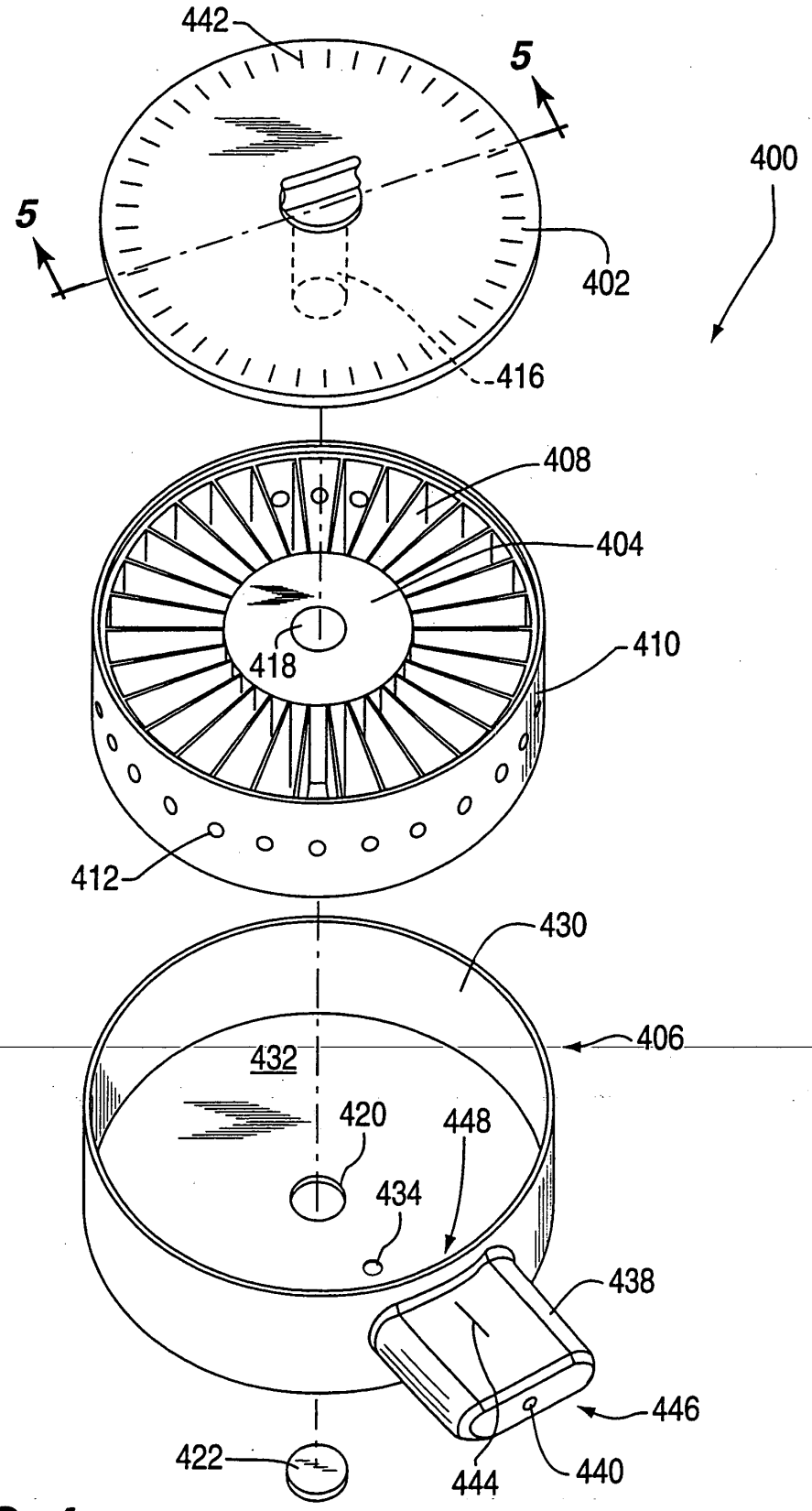

442
5
5
400
402
416
408
404
418
410
412
430
406
432
420
448
434
438
446
422
444
440

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/12222

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61M 15/00
US CL :128/202.21, 203.12, 203.15, 203.25; 239/102.1, 102.2; 604/58
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/202.21, 203.12, 203.15, 203.25; 239/102.1, 102.2; 604/58

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 2,534,636 (F. E. STIRN) 19 December 1950, see entire document.	1-10
Y	GB, A, 2 264 237 (NEWELL) 25 August 1993, see page 3 lines 4-9.	1-10
Y	WO, A, 90/13328 (HODSON ET AL.) 15 November 1990, see page 3 lines 34 and 35, page 4 lines 1-4, and page 64 lines 20-22.	1-10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 23 SEPTEMBER 1996	Date of mailing of the international search report 29 OCT 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3590	Authorized officer Stacia Sinnik for VIRENDRA SRIVASTAVA Telephone No. (703) 308-0959

Form PCT/ISA/210 (second sheet)(July 1992)*